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EXAMINER	
POHNERT, STEVEN C	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/565,847	PERUSSE ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/14/2008, 3/22/2007, 11/29/2006, 1/26/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The instant application is a national stage entry of PCT WO/05/012560 (application CA/04/001413). The claims of PCT WO/05/012560 were amended 12/12/2005 and marked as amended sheets and entered in the instant application on 1/26/2006. Thus claim 1-10 of the instant specification are pending and being examined.

Specification

1. The disclosure is objected to because of the following informalities:

The specification on page 5, line 15 recites, "□ gene". This appears to be a typographical error the rejection can easily be overcome by amending the specification to recite, "β gene."

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 9, line 4. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification recites on page 9, line 9 "(DNA or ARN)." This appears to be a typographical error and should be amended to recite, "(DNA or RNA)."

Appropriate correction is required.

Claim Objections

2. Claims 10 are objected to because of the following informalities:

Claim 10 does not end with a period and thus is improper. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors have been described by the court in re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in the Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

Claim 1 is drawn to a method of determining susceptibility or predisposition of "any" patient to "any" obesity comprising 1) identifying a "any" amino acid substitution of the neuromedin-β polypeptide or "any" nucleic acid in the neuromedin β encoding gene or 2) quantifying said nucleic acid sequence level , wherein in an alteration in the amino acid sequence or nucleic acid sequence compared to a normal patient is representative of predisposition or susceptibility to obesity.

The claims thus broadly encompass "any" patient which includes dogs, can humans, snakes, whales, etc.

Further the claims are drawn to "any" nucleic acid substitution or amino acid substitution in "any" neuromedin gene or polypeptide.

Claim 2 draws the invention to the nucleic acid sequence of SEQ ID NO 1 in which a cytosine is replaced with an adenine at position 217 of SEQ ID NO 1. Claim 3 is drawn to the result of the cytosine to adenine mutation in SEQ ID NO 1 at the protein level which results in the substitution of a threonine for the proline at position 73 of SEQ ID NO 2.

Claim 4 draws the claim invention to obesity as defined by body fatness, abdominal obesity and visceral obesity.

Claim 5 is drawn to a method for diagnosing a neuromedin-β associated eating disorder comprising a)characterizing the sequence or quantity of "nucleotide" encoding for neuromedin-β in a biological sample from a patient; b) determining the presence or absence of a nucleic or amino acid substation or quantity of said nucleic acid sequence

in the biological sample, wherein the substitution of at least one nucleotide or one amino acid in the sequence or "any" variation in the quantity of the said nucleotide or amino acid sequence or variation of quantity of said nucleotide compared to a normal patient is representative of the susceptibility of the an eating disorder.

Thus claim 5 requires the characterization or quantitation of a nucleotide- adenine, guanine, cytosine, uracil, thymine, etc. that is present in the gene or mRNA encoding Neuromedin b or wherein a substitution of one nucleotide or amino acid encoding neuromedin-b is indicative of susceptibility to eating disorders .

Claim 6 is drawn to the nucleotide sequence is DNA or RNA.

Claim 7 draws the invention to the eating disorder being disinhibition and susceptibility to hunger.

Claim 8 draws the invention to the nucleic acid sequence of SEQ ID NO 1 in which a cytosine is replaced with an adenine at position 217 of SEQ ID NO 1. Claim 9 is drawn to the result of the cytosine to adenine mutation in SEQ ID NO 1 at the protein level which results in the substitution of a threonine for the proline at position 73 of SEQ ID NO 2.

Claim 10 draws the invention to "said nucleotide encoding neuromedin-β is RNA nucleotide."

The amount of direction or guidance and the Presence and absence of working examples.

The specification teaches a longitudinal study was undertaken to examine genetics and obesity in Quebec (page 7, 1st paragraph). The specification teaches in

Table 1 that 274 men and 386 women were used in a genetic linkage study. The specification further teaches that the substitution of a cytosine at nucleotide 217 of SEQ ID NO 1 for an adenine results in a resultant change in amino acid 73 of SEQ ID NO 2 from a proline in wildtype to threonine in mutant (page 9, lines 8-16).

The specification further teaches amplification of a portion of a human nueromedin-b gene by use of SEQ ID NO 3 and SEQ ID NO 4 and minisequencing of position 217 of SEQ ID NO 1 by use of a primer of SEQ ID NO 5 (page 10, lines 7-11).

The specification further teaches eating behaviors were adjusted for age, gender and BMI (page 10, lines 13-14).

The specification teaches, "Men were less disinhibited than women and, for this reason, assignment to group of low or high disinhibition were performed for each gender separately. In men, cutoff values were 3 and 8 (0-3, 4-7 and 8-16), while in women the corresponding cutoffs were 4 and 10 (0-4, 5-9 and 10-16). For susceptibility to hunger, there where no gender differences and group assignments were the same in men and women with cutoff values of 2 and 6 (0-2, 3-6 and 4-14)" (page 11, lines 1-6).

The specification further teaches, "gastric tissues from each NMB c.217 C>A or p.P73T genotypes (total n=30) were randomly selected from a tissue bank of morbidly obese individuals" (page 11, lines 22-23). Thus the specification teaches the expression variation was determined only in patients that were morbidly obese.

The specification teaches, "For eating behaviors-related phenotypes, significant association was found between this mutation and disinhibition (p=0.0265, p=0.0057) and susceptibility to hunger (p=0.0343, p=0.0345) whether or not adjustment for BMI

was made (Table 3)"(page 13, last paragraph). The specification continues, "Cross-sectional studies also shown trends or significant association for BMI (p=0.0888), body fat (p=0.0357) and fat mass (p=0.0737), but not for macronutrient intake and energy intake or expenditure (Table 3)")"(page 13, last paragraph). The specification concludes page 13 by teaching the homozygous AA genotype frequency was higher in subjects with high disinhibition than those with low disinhibition and susceptibility to hunger.

Thus the specification teaches in table 3 that the AA genotype at position 217 of SEQ ID NO 1 was statistically correlated with disinhibition and susceptibility t hunger when compared to the CA or CC genotype. Thus the specification teaches that the homozygous presence of AA at position 217 of SEQ ID NO 1 is required for a predictable relationship. The specification teaches there is only a statistically significant correlation of the CA genotype with body fat and fat mass when compared the CC genotype in table 3. Thus the specification teaches that heterozygous CA genotype is predictably associated with body fat and fat mass only compared to the CC genotype.

The specification re-analyzes the data with respect to disinhibition and susceptibility to hunger in table 4 and again finds that subjects with the AA genotype were statistically more likely to have disinhibition (p=0.0381) and susceptibility to hunger (p=0.0154), compared to subjects with at least one C allele.

The specification on page 17 teaches, "The effect of the mutation on neuromedin-β gastric levels was not significant. However, as shown in Fig 6, the A/A homozygotes tends to have about 16.5% less NMB mRNA as compared to the C

carriers (70.3 +I 1.1 vs 86.5 +8.5;p=0.16). The neuromedin β c.217 C>A (p.P73T) polymorphism could explains as much as 7% of the variance of the gastric NMB mRNA levels." The specification previously taught these samples were from morbidly obese patients (page 11, lines 22-23). Thus the specification on page 17 teaches there is no statistical difference in the amount of nueromedin mRNA from gastric tissue of human subjects with different genotypes at position 217 of SEQ ID NO 1. However, the specification asserts on page 18, "This mutation was also associated with neuromedin-β gastric messenger RNA levels suggesting that neuromedin β gene expression or messenger RNA stability is compromised by the c.217 C>a (p.P73T) substitution." Thus the specification appears to be contradicting itself as page 17 says there is no significant association of the mutation with mRNA, while on page 18 stating there is an association between the mutation and mRNA.

The specification does not provide a working example in which quantitation of neuromedin-β mRNA levels is associated with obesity or any eating disorders. It would thus be unpredictable to correlate altered expression of variants of neuromedin-β with obesity or eating disorders without specific guidance by the specification.

The specification provides no examples or guidance as to the use of the instant method in subjects other than humans.

The specification provides no guidance as to any variation of neuromedin β nucleic or protein sequence other than the mutation of position 217 of SEQ ID NO 1 is correlated with obesity or eating disorders.

The specification provides no guidance for the detection of a mutation at position 73 of SEQ ID NO 2, other than indirectly through the detection of the nucleic acid sequence. Thus the specification does not teach methods of detecting mutations in the protein.

The specification provides no data as to the effect of any mutation of neuromedin-β on visceral or abdominal obesity. The specification provides no data, guidance or nexus to suggest that the instant mutation is predictably associated with dietary restraint, binge eating disorders, bulimia nervous or anorexia nervousa.

The state of prior art and the predictability or unpredictability of the art:

Oeffner et al (Acta Diabetol (2000) volume 37, pages 93-101) teaches a study investigating the role of neuromedin β mutations on obesity (see abstract). Oeffner teaches neuromedin β is tanscribed as two mRNA of approximately 800 bases in length that are widely distributed (page 95, 1st column, 1st full paragraph). Oeffner teaches that a transversion found at position 253 C>A resulted in a substitution at position 73 for a threonine for a proline (instant claims)(page 97, 2nd column, 1st paragraph). Oeffner teaches there was no association between the 253C>A mutation and body weight (obesity) (P=0.98) (page 97, 2nd column, 2nd full paragraph and table 2). Oefner teaches there was an association of a 401C>A mutation with body weight comparing 92 extremely obese patients to 94 underweight controls (p=0.031)(page 97, 2nd column, 3rd paragraph). Oeffner teaches this 401C>A is silent mutation was validated in a second sample with a p value of 0.024 (page 99, 1st column last paragraph). Thus Oeffner teaches that "any" mutation in nueromedin β is not

predictably associated with obesity or body weight as the 253C>A was not found to be affected, while the 401 C>A was found to be correlated with body weight.

Post-filing art, Spalova et al (Physiological Reviews (2008) volume 57, pages S39-S48) presents a study to examine the correlation of the P73T polymorphism in subjects of Czech descent before and after a longitudinal weight reduction program. Spalova teaches a study comparing 37 obese men and 255 obese women with 51 normal weight men and 104 normal eight women (s40, 2nd column, 1st paragraph). Spalova teaches in table 2 there was no significant differences in genotypes at position 73 between obese and normal people (p=0.353). Spalova teaches that male T non-carriers (wildtype males) had a higher hunger score prior to the weight reduction program (p=0.015)(page 42, 2nd column last paragraph). Spalova teaches non-T carriers had a greater weight loss on average than carriers although not statistically significant (page S42, 2nd column, last paragraph). Spalova in the discussion addresses that their finding are consistent with Oeffners but inconsistent with applicant's post-filing art with respect to genotypes and body weight (page S43, 2nd column 2nd paragraph). Spalova denotes that applicant's prost-filing art may be due to experimental differences in Eating inventory analysis (s46, 1st column, 1st paragraph). Spalova further suggests the differences between the post filing art of instant inventors and Spalova study may include ethnicity, age, BMI and duration of follow up.

Brenner et al (Trends in Genetics (2001) volume 17, pages 414-418) teaches that, "Here, the 'homology-implies-equivalency' assumption is restricted to a subset of homologs that diverged in the most-recent common ancestor of the species sharing the

homologs. This strategy is useful, of course. But it is likely to be far less general than is widely thought. Two species living in the same space, almost by axiom, cannot have identical strategies for survival. This, in turn, implies that two orthologous proteins might not contribute to fitness in exactly the same way in two species" (see page 414, 3rd column last full paragraph). Brenner specifically describes that although the leptin gene homologs have been found in mice and humans, their affect is different (see page 414, 3rd column last paragraph-3rd column page 415). Brenner specifically teaches that the leptin gene in mice plays a major role in obesity, but no such effect has been demonstrated in humans due perhaps to the different evolutionary forces. Brenner thus teaches that the activity and function of genes in different species is unpredictable.

The art teaches genetic variations and associations are often irreproducible. Hirschhorn et al. (Genetics in Medicine. Vol. 4, No. 2, pages 45-61, March 2002) teaches that most reported associations are not robust. Of the 166 associations studied three or more times, only 6 have been consistently replicated. Hirschhorn *et al.* suggest a number of reasons for the irreproducibility of studies, suggesting population stratification, linkage disequilibrium, gene-gene or gene-environment interactions, and weak genetic effects and lack of power are possible factors that lead to such irreproducibility. Hirschhorn *et al.* caution that the current irreproducibility of most association studies should raise a cautionary alarm when considering their use as diagnostics and prognostics (p. 60, Col. 2). Thus, Hirschhorn cautions in drawing conclusions from a single report of an association between a genetic variant and disease susceptibility.

The art teaches that presence of SNPs in the same gene does not indicate that each of the genes is associated with the same diseases. Meyer et al. (PG Pub 2003/0092019), for example, teaches that SNPs in the CADPKL gene are not each associated with neuropsychiatric disorders such as schizophrenia. Specifically Meyer teaches that cadpkl5 and cadpkl6 are not associated with the disease, however cadpkl7 has a p-value of less than 0.05, therefore an association exists (see table 5). Each of these polymorphisms are SNPs within the CADPKL gene, however, it is apparent that they are not all associated in the same manner with disease. Thus, Meyer exemplifies that the association of a single SNP in a gene does not indicate that all SNPs within the gene are associated with the disease.

Further, it is relevant to point out that in general the art is highly unpredictable with regard to the functionality of a given genomic polymorphism. After a polymorphism is identified, it is unpredictable whether any such polymorphism would be associated with any phenotypic trait in every population. For example, Hacker et al teaches that they were unable to confirm an association between a gene mutation and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (see abstract, Gut, 1997, Vol. 40, pages 623-627). Additionally, post-filing art reveals that most gene association studies are typically wrong. Lucentini (The Scientist, 2004, page 20) teaches that it is strikingly common for follow-up studies to find gene-disease associations wrong (left column, 3rd paragraph). Lucentini teaches that two recent studies found that typically when a finding is first published linking a given gene to a disease there is only roughly a

one-third chance that the study will reliably confirm the finding (left column, 3rd paragraph). Lucentini teaches that bigger sample sizes and more family-based studies, along with revising statistical methods, should be included in the gene association studies (middle column, 1st complete paragraph).

Vandesompele teaches, " Accurate normalization of gene expression levels is an absolute prerequisite for reliable results, especially when the biological significance of subtle gene expression differences is studied" (see page 9, 2nd column, discussion) (Vandesompele et al (Genome Biology (2002) volume 3 , pages 1-11). Vandesompele teaches, " That the conventional use of a single gene normalization leads to relatively large errors in a significant portion of samples tested" (see abstract, results). Vandesompele teaches that ACTB (beta actin) appears to be the one of the worst genes for normalization and thus resulting in large normalization errors (see page 10, 1st paragraph). Vandesompele teaches at least 3 housekeeping genes are required for accurate normalization (see page 10, 1st column, 1st full paragraph). Vandesompele thus teaches that studies of gene expression using a single gene for normalization are unpredictable due to the large variation in the expression of the genes used for normalization.

The art of Cheung et al (Nature Genetics, 2003, volume 33, pages 422-425) teaches that there is natural variation in gene expression among different individuals. The reference teaches an assessment of natural variation of gene expression in lymphoblastoid cells in humans, and analyzes the variation of expression data among individuals and within individuals (replicates) p.422, last paragraph; Fig 1). The data

indicates that, for example, expression of ACTG2 in 35 individuals varied by a factor of 17; and that in expression of the 40 genes with the highest variance ratios, the highest and lowest values differed by a factor of 2.4 or greater (Fig 3).

The level of skill in the art:

The level of skill in the art is deemed to be high

Quantity of experimentation necessary:

In order to practice the invention as claimed, one would first have to establish that a predicative relationship exists between the presence of “any” amino acid or “any” nucleotide substitution in any neuromedin β gene and predisposition or susceptibility to obesity or obesity related eating behavior. As the specification teaches a single mutation at position 217 C>A in SEQ ID NO 1 of the human nueromedin β gene is associated with body fat mass, this finding is contradicted by the pre-filing art of Oeffner as well as the post-filing art of Spalova, which found no correlation with body mass or fat mass, respectively. Thus it would be unpredictable to associate “any” mutation in nueromedin-β with obesity when there are suggests such a relationship is not reproducible and thus unpredictability.

Further as the specification teaches there was no statistical correlation for BMI or fat mass, but only body fat, it would be unpredictable associate “any" type of obesity with the presence of “any” mutation in the nueromedin β or even the specific mutation taught by the instant specification due to the conflicting data of the Oeffner and Spalova.

Further it would be unpredictable to use "any" mutation of neuromedin β as representative of disinhibition or susceptibility to hunger as Spalova could not confirm

the effect in a Czech population and actually found that subjects that did not carry the mutant allele were more likely to have disinhibition and hunger, which contradicts the instant specification which teaches in table 3 the homozygous mutant genotype had a greater susceptibility to hunger.

Further it would be unpredictable to use the quantity of variants of neuromedin-B mRNA from as a method for determining the susceptibility of a subject to obesity as the specification provided no evidence that level of expression of neuromedin is correlated with obesity, but provided a single study in which the expression of the variants of nueromedin were examined in samples from morbidly obese gastric patients and found no correlation between genotype and expression levels. Thus as the specification has provided no data to suggest that nueromedin b expression is correlated in any tissue with obesity it would be unpredictable to determine susceptibility without such guidance. Further there is no suggest in the specification that gastric expression of neuromedin β is indicative of expression in any other tissue thus it would be unpredictable to use any tissue without first determining there is a correlation in the expression of nueromedin and obesity in that tissue.

In order to practice the invention of claim 6, to the susceptibility of eating disorders, one would first have to establish that a predicative relationship exists between the sequence or quantity of nucleotide encoding for neuromedin or the amino acid sequence of and determining the presence of a nucleic acid substitution or quantity of said nucleic acid sequence . Thus the claims broadly encompass determining if there is a variation in the amount of any nucleotide that is present in nueromedin β in a

sample or a sequence variation. The specification provides no guidance as to the effect of nucleotide content of a sample and eating disorders. Thus it would be unpredictable to make such a correlation without specific guidance. Although, the specification teaches detection of nueromedin β variants in gastric tissue of morbidly obese patients it does not teach there is a statistical correlation, or the variants are correlated with eating disorders. Thus it would be unpredictable to extrapolate from the teachings of a study of morbidly obese subjects to eating disorders without specific guidance that such a correlation exists. Further while the specification teaches there is a correlation of the homozygous AA genotype to disinhibition and susceptibility to hunger Spalova (post filing art) could not replicate this finding. Thus the artisan could not predictably perform the instant invention as claimed as the art of Hirschhorn and Lucentini recognized prior to the time of filing that genetic studies are generally not reproducible and thus not predictable until replication has occurred.

The claims to expression analysis would be further unpredictable as Cheung and Vandesompele teach that there is great variation in gene expression between individuals and multiple normalization controls are required for reproducible data.

Additionally, it would be unpredictable to extrapolate the method of the instant claims to any other species or any other mutations in the nueromedin-β gene in view of the teachings of Brenner and Meyer. Specifically Meyer teaches that due to different evolutionary pressures genes in different species often have slightly different functions, thus it would be unpredictable to extrapolate an association found in one species to another species without confirmation that such an association is present. Further Meyer

teaches that “any” mutation in a gene does not predictably result in the same phenotype as other mutations in the gene.

Therefore, in light of the breadth of the claims, the lack of guidance in the specification, the high level of unpredictability in the associated technology, the nature of the invention, the negative teachings in the art, and the quantity of unpredictable experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention as claimed.

5. Claims 1 and 4-7 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to methods of detecting “any” variation in “any” nucleic acid or “any” amino acid in “any” neuromedin-b gene from “any” species. Claims 2-3 and 9-10 are not being rejected as they are limit the invention to specific sequences.

When the claims are analyzed in light of the specification, the invention encompasses an enormous number of nucleotide molecules. The specification teaches the nucleic acid sequence of human neuromedin-b in SEQ ID NO 1, and the amino acid sequence of human nueromedin-b in SEQ ID NO 2. The specification teaches in figure 7 the sequence of 11 SNPs of the human nueromedin-B gene. The specification does not teach the sequence of nueromedin-b in any other species. Further the specification does not limit the instant invention to humans.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been by full structure. The instant specification teaches the nucleic acid sequence of human neuromedin-b in SEQ ID NO 1, and the amino acid sequence of human nueromedin-b in SEQ ID NO 2. The specification teaches in figure 7 the sequence of 11 SNPs and wildtype sequences of the human nueromedin-B gene (SEQ ID NO 14-35).

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. other nucleotide sequences or positions with in a specific gene or nucleic acid), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case the specification provides no structural limitations for the genus of neuromedin-b genes or broad genus of nucleic acid or amino acid substitutions. The claims read in light of the specification encompass any nucleic acid molecule from any species that can broadly be identified as a neuromedin-b gene or a mutated neuromedin-b nucleic acid or polypeptide. While the teaches of the specification describes 11 SNPs, it only asserts one of these sequence variations is indicative of nueromedin b gene that results in predisposition to obesity or obesity associated eating disorders, and provides no guidance in the form of a structure function relationship to the artisan as to how to a priori determine any other nucleotide substitution that results in the phenotypes of the claims.

Neuromedin B genecard NMB gene protein coding GC15M082999 (www.genecards.org/cgi-bin/carddisp.pl?gene=NMB&search=neuromedin+b&suff=txt,

10/23/2008, pages 1-11) teaches there are 2 splice variants of Neuromedin B and 595 known cDNA. Neuromedin B gene card teaches a homolog to the human neuromedin has been identified in 5 species.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids, polypeptides and polymorphisms that are broadly encompassed by the recitation of neuromedin-B regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In

re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

In the instant application, the provided information regarding nucleic acid and polypeptide of Neuromedin b in any species, do not constitute an adequate written description of the broad subject matter of the claims, and so one of skill in the art cannot envision the detailed chemical structure of the nucleic acids encompassed by the claimed nucleic acids, polypeptides and variants thereof. Adequate written description requires more than a statement that nucleic acids with a particular quality are part of the invention and reference to a potential method for their identification. The nucleic acid sequence is required.

In conclusion, the limited information provided regarding neuromedin b nucleic acids, proteins, and variants is not deemed sufficient to reasonably convey to one skilled in the art nucleic acid molecules the molecules claimed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 1recites, "said obesity being representative of disinhibition or susceptibility or predisposition to hunger or eating behavior disorders." It is unclear if the claim is defining obesity as limited to "disinhibition or susceptibility or predisposition to hunger or eating behavior disorders," or if the claim is merely stating that that disinhibition or susceptibility or predisposition to hunger or eating behavior disorders are encompassed by obesity. It is thus unclear what the intended metes and bounds of the claims are. Claim 2-4 depend from claim 1 and as thus rejected as the have every limitation of the claim from which they depend.

9. Claim 5 recites the limitation "said characterized biological sample" in step a. The claim 5 does not previously recite "characterized biological sample." Thus there is insufficient antecedent basis for this limitation in claim 5 and all claims which depends from it (claims 6-10). This rejection said easily be overcome by amending the claims to recite "said biological sample.

Claim 5 further recites, " nucleotide encoding for neuromedin b" in step a. "Nucleotide" in the art generally refers to a single adenine, guanine, thymine or uracil, it is thus unclear how a single nucleotide encodes a gene such as neuromedin-b. This rejection can easily be overcome by amending step a of claim 5 to recite, "characterizing of neuromedin-b nucleic acid sequence or the quantity of neuromedin-B

nucleic acid sequence in the biological sample. Claims 6-10 depend from claim 5 and thus require all the limitations of claim 5 and are rejected.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Oeffner et al (Acta Diabetol (2000) volume 37, pages 93-101).

This rejection is drawn to the breadth of the instant claims and is consistent with the enablement rejection as it is drawn to an embodiment that is encompassed by the breadth of claim 1, but is not disclosed in the instant application.

Claim 1 is drawn to a method of detecting obesity by identifying an alteration in the nucleotide sequence, amino acid sequence or quantity of neuromedin b in a subject relative to a normal patient, wherein a variation in sequence or decrease in expression of nueromedin-b is representative of predisposition or susceptibility obesity, said obesity being representative of disinhibition or susceptibility or predisposition to hunger or to eating behavior disorders. As it is unclear if the claim language of "said obesity being representative of disinhibition or susceptibility or predisposition to hunger or to eating behavior disorders" is intended to limit obesity to disinhibition of hunger or eating behavior disorders, the claims are being given the broadest reasonable interpretation the obesity includes disinhibition of hunger or eating behavior disorders.

Oeffner teaches a study investigating the role of neuromedin B mutations on obesity (see abstract). Oeffner teaches neuromedin b was amplified in sequenced in samples to determine mutations (page 96, 2nd column last paragraph to page 97). Oeffner teaches there was an association of a 401C>A mutation of neuromedin b with body weight comparing 92 extremely obese patients to 94 underweight controls ($p=0.031$)(page 97, 2nd column, 3rd paragraph). Oeffner teaches this 401C>A is silent mutation was validated in a second sample with a p value of 0.024 (page 99, 1st column last paragraph). Thus Oeffner teaches identifying a nucleic acid substitution in the gene encoding neuromedin b, wherein the substitution correlated with obesity and thus anticipates the claim.

Summary

No claims are allowed.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steven C Pohnert/
Examiner, Art Unit 1634

Steven Pohnert